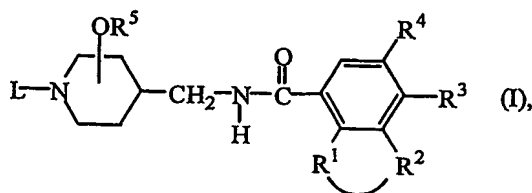


Claims

1. A compound of formula (I)



a stereochemically isomeric form thereof, an *N*-oxide form thereof, or a pharmaceutically acceptable acid or base addition salt thereof, wherein -R¹-R²- is a bivalent radical of formula

-O-CH₂-O- (a-1),

-O-CH₂-CH₂- (a-2),

-O-CH₂-CH₂-O- (a-3),

-O-CH₂-CH₂-CH₂- (a-4),

-O-CH₂-CH₂-CH₂-O- (a-5),

-O-CH₂-CH₂-CH₂-CH₂- (a-6),

-O-CH₂-CH₂-CH₂-CH₂-O- (a-7),

-O-CH₂-CH₂-CH₂-CH₂-CH₂- (a-8),

wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C₁₋₆alkyl or hydroxy,

R³ is C₁₋₆alkyl, C₁₋₆alkyloxy, or halo;

R⁴ is hydrogen or halo;

provided that when R³ and R⁴ are both halo, then the bivalent radical-R¹-R²- is of formula (a-5);

R⁵ is hydrogen or C₁₋₆alkyl, and the -OR⁵ radical is situated at the 3- or 4-position of the piperidine moiety;

L is hydrogen, or L is a radical of formula

-Alk-R⁶ (b-1),

-Alk-X-R⁷ (b-2),

-Alk-Y-C(=O)-R⁹ (b-3), or

-Alk-Z-C(=O)-NR¹¹R¹² (b-4),

wherein each Alk is C₁₋₁₂alkanediyl; and

R⁶ is hydrogen; hydroxy; cyano; C₃₋₆cycloalkyl; C₁₋₆alkylsulfonylamino; aryl or Het;

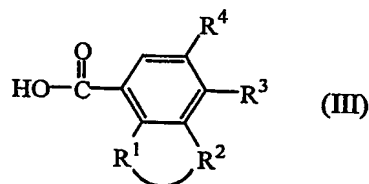
R⁷ is C₁₋₆alkyl; C₁₋₆alkyl substituted with hydroxy; C₃₋₆cycloalkyl; aryl or Het;

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- X is O, S, SO₂ or NR⁸; said R⁸ being hydrogen or C₁₋₆alkyl;
 R⁹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, hydroxy or aryl;
 Y is a direct bond, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
 Z is a direct bond, O, S, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
 5 R¹¹ and R¹² each independently are hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, or R¹¹ and R¹² combined with the nitrogen atom bearing R¹¹ and R¹² may form a pyrrolidiny, piperidiny, piperaziny or 4-morpholinyl ring both being optionally substituted with C₁₋₆alkyl;
 10 aryl represents unsubstituted phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, nitro, trifluoromethyl, amino, aminocarbonyl, and aminosulfonyl; and
 Het is furanyl; furanyl substituted with C₁₋₆alkyl or halo;
 15 tetrahydrofuranyl; tetrahydrofuranyl substituted with C₁₋₆alkyl;
 dioxolanyl; dioxolanyl substituted with C₁₋₆alkyl;
 dioxanyl; dioxanyl substituted with C₁₋₆alkyl;
 tetrahydropyranyl; tetrahydropyranyl substituted with C₁₋₆alkyl;
 2,3-dihydro-2-oxo-1H-imidazolyl; 2,3-dihydro-2-oxo-1H-imidazolyl
 20 substituted with one or two substituents each independently selected from halo, or C₁₋₆alkyl;
 pyrrolidiny; pyrrolidiny substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
 pyridiny; pyridiny substituted with one or two substituents each independently selected from halo, hydroxy, C₁₋₆alkyl;
 25 pyrimidiny; pyrimidiny substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
 pyridaziny; pyridaziny substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo;
 30 pyraziny; pyraziny substituted with one ore two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo.
2. A compound as claimed in claim 1 wherein the -OR⁵ radical is situated at the 3-position of the piperidine moiety having the trans configuration.
 - 35 3. A compound as claimed in claim 2 wherein the absolute configuration of said piperidine moiety is (3S, 4S).

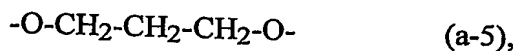
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4. A compound as claimed in any of claims 1 to 3 wherein -R¹-R²- is a radical of formula (a-5), R³ is chloro and R⁴ is chloro.
5. A compound as claimed in any of claims 1 to 3 wherein -R¹-R²- is a radical of formula (a-5), R³ is chloro and R⁴ is bromo.
6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 5.
7. A process for preparing a pharmaceutical composition according to claim 6 wherein a therapeutically active amount of a compound according to any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.
8. A compound according to any of claims 1 to 5 for use as a medicine.
9. A compound of formula (III).



wherein

-R¹-R²- is a bivalent radical of formula

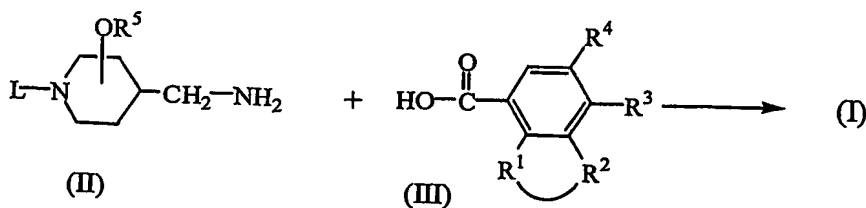


wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C₁₋₆alkyl or hydroxy;

R³ is C₁₋₆alkyl, C₁₋₆alkyloxy, or halo; and

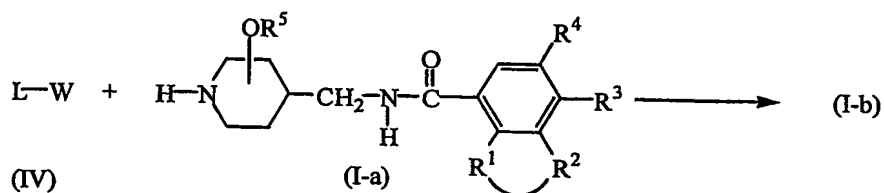
R⁴ is hydrogen or halo.

10. A process for preparing a compound of formula (I) wherein
- a) an intermediate of formula (II) is reacted with an carboxylic acid derivative of formula (III) or a reactive functional derivative thereof;

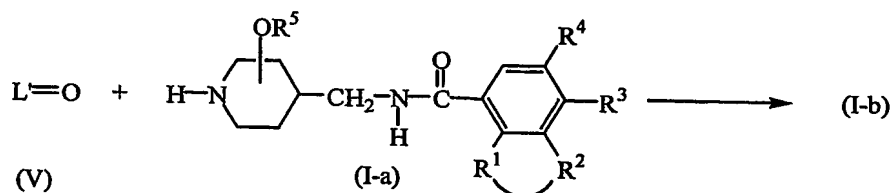


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- b) an intermediate of formula (IV) is *N*-alkylated with a compound of formula (I-a), defined as a compound of formula (I) wherein L represents hydrogen, in a reaction-inert solvent and, optionally in the presence of a suitable base, thereby yielding compounds of formula (I-b), defined as compounds of formula (I) wherein L is other than hydrogen;



- c) an appropriate ketone or aldehyde intermediate of formula L'=O (V), said L'=O being a compound of formula L-H, wherein two geminal hydrogen atoms in the C₁₋₁₂alkanediyl moiety are replaced by =O, is reacted with a compound of formula (I-a), thereby yielding compounds of formula (I-b);



wherein in the above reaction schemes the radicals -R¹-R²-, R³, R⁴ and R⁵ are as defined in claim 1 and W is an appropriate leaving group;

- d) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.